

Therapies for Advanced Heart Failure: Therapies on the Horizon

**Daniel Burkhoff MD PhD
Adjunct Associate Professor of Medicine
Columbia University**

Acute Cardiogenic Shock (CGS)

Mortality: >40%

Prior Studies:

Approaches

IABP

Percutaneous Support with 3.5L/min device

iNOS Inhibitors

Cooling (planned, but negative wrt MI size reduction)

Results

Improved (but not normalized) hemodynamics

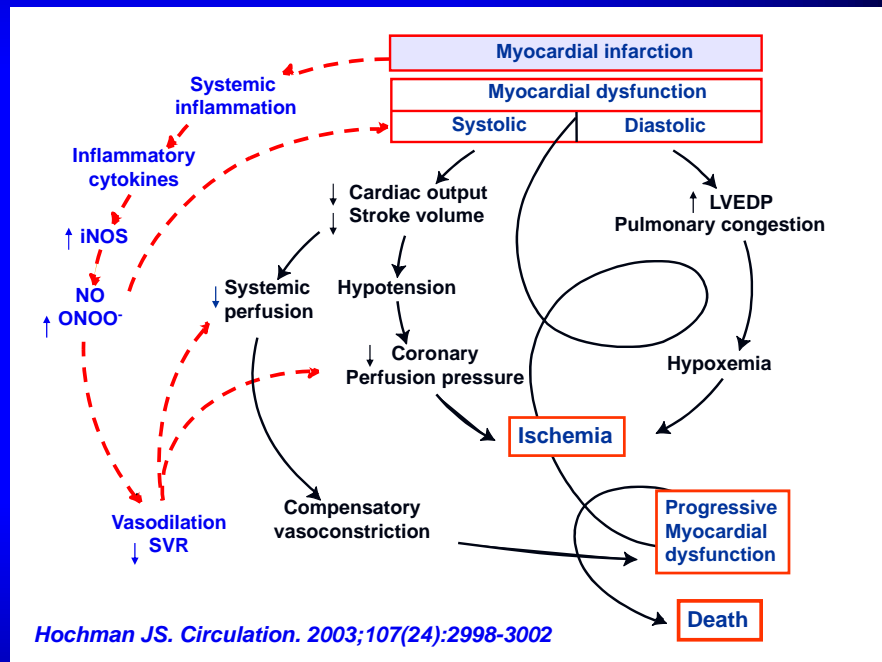
Negative wrt to mortality

Opportunities:

Percutaneous full support ($\geq 5\text{L/min}$) device

Combination of hemodynamic support plus

iNOS inhibition



Facilitated Myocardial Recovery: LVADs+Drugs

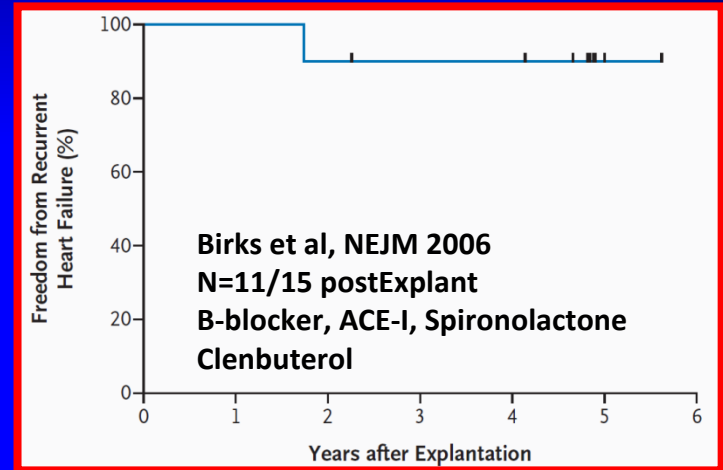
Left Ventricular Assist Devices (LVADs) normalize BP, CO, neurohormonal milieu and unload the LV. These effects induce marked **reverse remodeling**.

Use of standard therapies in combination with a β -agonist during LVAD support has been reported by one group to permanently normalize LV function so that LVADs can be removed: *bridge-to-recovery*.

These findings could not be reproduced in one multicenter study.

Opportunity:

Evaluate differences in conduct of prior studies and assess value of repeating a multicenter study, versus supporting additional basic research.



Cardiac Improvement During
Mechanical Circulatory Support
Maybaum et al, 2007;115:2497

Conclusions: Cardiac function improves significantly after device implantation. Although cellular recovery and improvement in ventricular function are observed, the degree of clinical recovery is insufficient for device explantation in most patients with chronic heart failure.

Right Heart Failure during LVAD Support

Right heart failure (RHF) requiring intervention is emerging as an important SAE in LVAD patients, with an incidence generally reported between 10-25% of patients.

Extracorporeal VADs have been the traditional approach but, as the need for increasingly long durations of RV, investigators have adapted currently available LVADs for this purpose.

Opportunities:

- Better understanding of the pathophysiology of RHF (pulmonary, cardiac, other factors)
- Better understanding of the risk factors predisposing to RHF
- Customized devices for right heart support



Loforte A. et al.; *Interact CardioVasc Thorac Surg*
2011;12:458-460

Other Areas of Interest

SVR (STICH Hypothesis 2)

Results were reported as decidedly negative

However:

- Many aspects of the study have been criticized
- 13% without h/o MI; 50% with a- or dyskinesia
- Smaller than protocol-intended reduction in LV size

LVADs for Children and Infants

NIH has a long history of supporting pediatric VADs

Baldwin JT, et al. The national heart, lung, and blood institute pediatric circulatory support program: a summary of the 5-year experience. *Circulation* 2011;123:1233-1240

Partial vs Full Hemodynamic Circulatory Support

Continuous Flow devices (which provide full hemodynamic support 5-9 L/min) have made major advances over prior generation, larger pulsatile devices in terms of SAEs and mortality

Efforts underway to perfect even smaller pumps for “less sick” patients (INTERMACS≤4)

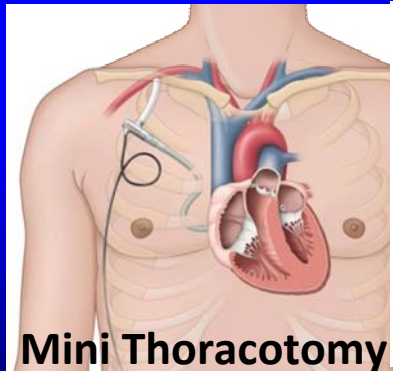
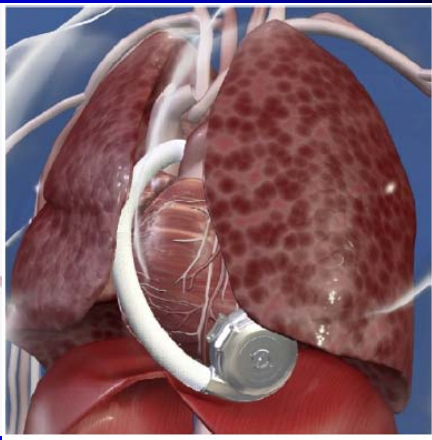
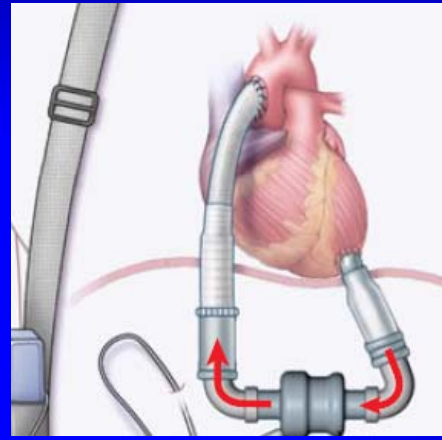
Smaller pump ⇒ Less flow

(4.25L/min)

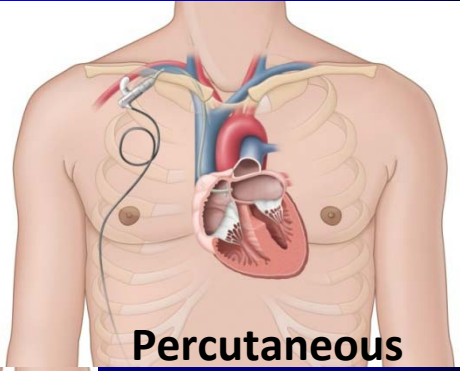
Has the potential for percutaneous implant which should theoretically further reduce procedural complications

Opportunities

Hemodynamic and clinical benefits of partial support



Mini Thoracotomy



Percutaneous